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Case Report

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Sotorasib-Induced Bullous Pemphigoid in a Patient with Non-Small Cell Lung Cancer

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Abstract

Bullous pemphigoid (BP) is an autoimmune subepidermal blistering disorder typically seen in the older adults, characterized by tense bullae and intense pruritus. Although BP can be idiopathic, medications are being increasingly recognized as their triggers. Sotorasib, is a KRAS G12C inhibitor approved for the non-small cell lung cancer (NSCLC) treatment; it can have associated dermatologic side effects; however, the reports of BP induced with this drug are almost non-existent. We present a unique case of Sotorasib-induced BP in a patient with advanced NSCLC, highlighting the importance of recognizing this potential cutaneous complication in the patients receiving novel targeted therapy [1].

Keywords: Sotorasib, Bullous Pemphigoid, Non-Small Cell Lung Cancer (NSCLC)

1. Introduction

Sotorasib, marketed as Lumykras®, is the first FDA-approved KRAS G12C inhibitor for the treatment of non-small cell lung cancer (NSCLC) with KRAS G12C mutations. While it represents a significant advancement in cancer treatment, it is associated with a variety of side effects affecting multiple systems.Gastrointestinal symptoms are among the most prevalent adverse effects associated with Sotorasib. Diarrhoea stands out as the most frequently reported, impacting up to 42% of patients, often presenting as a significant management challenge. Nausea, vomiting, constipation, and abdominal pain, though commonly observed, are generally less severe and manageable with supportive care [2]. Hepatotoxicity is another critical concern, characterized by elevations in liver enzymes (ALT and AST) in approximately 25% of patients. Such changes can necessitate dose modifications or even discontinuation of the drug in severe cases.Respiratory adverse effects include cough and dyspnoea, which, while generally mild, are notable. Rare but potentially life-threatening conditions like interstitial lung disease (ILD) or pneumonitis have also been documented, underscoring the need for careful monitoring of respiratory symptoms [3]. Musculoskeletal issues, particularly musculoskeletal pain and arthralgia are reported in roughly 35% of cases. These symptoms can significantly affect patient tolerability and may require tailored pain management strategies.Fatigue, including general tiredness and asthenia, is a common side effect affecting approximately 26% of patients. This symptom can profoundly impact the quality of life, emphasizing the importance of addressing patient well-being during treatment. Dermatologic Reactions: Rashes are reported in up to 12% of patients. These are typically mild but may contribute to overall discomfort [1]. Few dermatological side effects were reported in the prescribing information for Sotorasib in patients with non-small cell lung cancer (NSCLC). These included dermatitis, acneiform dermatitis, maculopapular rash, and pustular rash [4,5].

However, the development of Bullous pemphigoid as a side effect of Sotorasib was not explicitly mentioned in the literature.

In contrast, several paraneoplastic skin manifestations of lung cancers have been reported, including plantar hyperkeratosis, Erythema gyratumrepens, acanthosis palmaris, Trousseau's syndrome, and erythroderma [6]. However, Bullous pemphigoid was not listed in the literature as dermatological manifestations of lung cancers.

Bullous pemphigoid is an autoimmune blistering disease that primarily affects elderly patients. This condition is marked by autoantibodies against hemi-desmosomal components BP180 and BP230, leading to subepidermal blistering [7,8]. Drug-induced BP is well-documented with agents such as dipeptidyl peptidase-4 (DPP-4) inhibitors and Programmed Death-1 inhibitors (PD-1 inhibitors).

In this review, we will highlight a confirmed case of bullous pemphigoid disease following the use of Sotorasib in the treatment of NSCLC.

2. Case Presentation

A 68-year-old male with stage IVA recurrent metastatic right upper lobe lung adenocarcinoma, positiveKRAS G12C-mutatation, (pT2a, N3 M1b) right axillary lymph node metastasis. He had 10-20% positive of PD-L1(Programmed Death-Ligand 1).Other mutations were negative including EFGR (Epidermal Growth Factor Receptor), ALK (Anaplastic Lymphoma Kinase), ROS1(ROS Proto-Oncogene 1, Receptor Tyrosine Kinase), BRAF (B-Raf Proto-Oncogene, Serine/Threonine Kinase), MET (MET Proto-Oncogene, Receptor Tyrosine Kinase), RET (Rearranged During Transfection) and NTRK (Neurotrophic Tyrosine Receptor Kinase).

The patient completed 7 cycles of palliative Pembrolizumab in April ‘24, switching to a six-weekly dosing after cycle 6; and started on Sotorasib during cycle 2.

Patientpresented to our dermatology clinic withwidespread pruritic bullous lesions during theSotorasibtreatment.He denied similar dermatologicalsymptoms in the past. He did not report any significant allergies or any hypersensitivity to any medications. He denied any family history of any skin disease.

On physical examination, the patient exhibited multiple widespread tense bullae on erythematous bases, particularly on the trunk and extremities. There were no mucosal lesions, the patient reported intense pruritus that significantly impacted his quality of life. Initial differential diagnoses included Bullous Pemphigoid, pemphigus vulgaris, and drug-induced linear IgA bullous dermatosis.

3. Diagnostic Workup & Management

Laboratory studies showed peripheral eosinophilia (eosinophils, 12%). Serology for basement membrane antibodies were positive. A lesional biopsy revealed a subepidermal bulla with an inflammatory infiltrate rich in eosinophils, suggestive of BP. Direct immunofluorescence of perilesional skin demonstrated linear IgG and C3 deposition along the basement membrane zone, consistent with BP [9,10].

Given the patient’s oncologic dependence on Sotorasib, a shared decision with the oncologist was made to continue the medication while managing BP symptomatically. The patient was initiated on oral corticosteroids (clobetasol 0.05%) and systemic doxycycline (100 mg twice daily) to mitigate inflammation.

Within four weeks, there was significant improvement in pruritus and in new blister formation. Follow-up BP180 and BP230 antibody levels demonstrated a modest decline, correlating with clinical improvement [11].

Despite the initial improvement after treatment, the patient continued to experience periodic mild flares of vesicular lesions that were managed effectively with the symptomatic treatment. The vesicular rash was in complete remission once the patient discontinued the Sotorasib between the treatment cycles. During the 3rd cycle the patient fell ill and decided himself to stop the drug and the lesions subsided completely, until restarting the drug and the lesions reappeared.

Based on the strong temporal relationship of rash occurrence with the initiation of Sotorasib, and its disappearance upon drug’s withdrawal; accompanied by the characteristic biopsy & immunofluorescence findings, a diagnosis of sotorasib-induced BP was established.

4. Discussion

This case represents a rare instance of Sotorasib-induced BP. Drug-induced BP is most frequently reported with DPP-4 inhibitors and immune checkpoint inhibitors, but targeted therapies such as Sotorasib are now implicated in the disease’s pathogenesis. The exact mechanism by which Sotorasib triggers BP remains unclear, though immune dysregulation and cytokine imbalance may play a role in predisposing individuals to autoantibody formation against BP antigens [12-14].

The temporal relationship between Sotorasib initiation and BP onset, combined with characteristic histopathologic and immunofluorescent findings, supports a causal association. In this patient, BP was successfully managed while maintaining Sotorasib therapy, demonstrating that symptomatic management can be effective when discontinuation of the triggering agent is not feasible.

5. Conclusion

With the increasing use of targeted therapies, dermatologic adverse effects, including rare autoimmune reactions, are becoming more prevalent. Clinicians should remain vigilant for signs of BP in patients on sotorasib, as timely diagnosis and appropriate management can significantly improve patient quality of life without necessitating discontinuation of life-prolonging cancer

treatments. Further studies are warranted to explore the underlying mechanisms and establish management guidelines for sotorasib-induced BP [15].

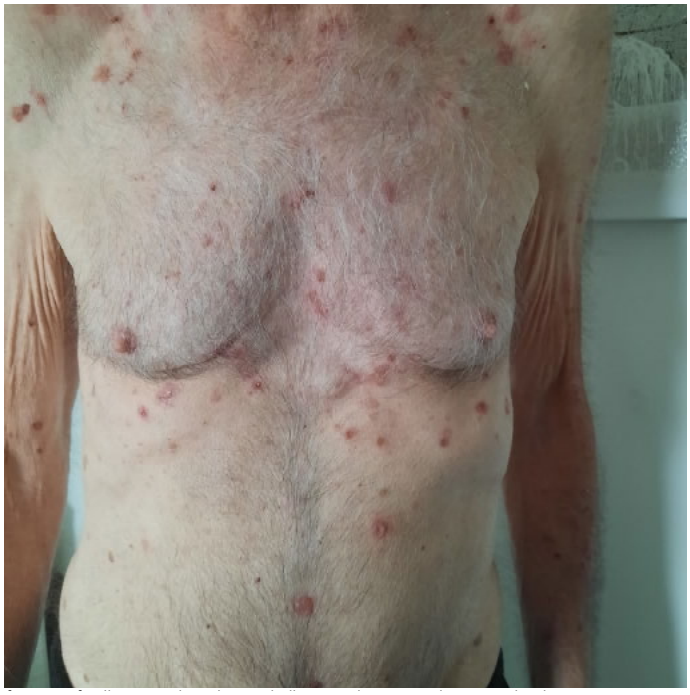

Figure 1: Clinical Features of Bullous Pemphigoid, Tense Bulla on Erythematous Plaques on the Chest, Upper Arms and Abdomen

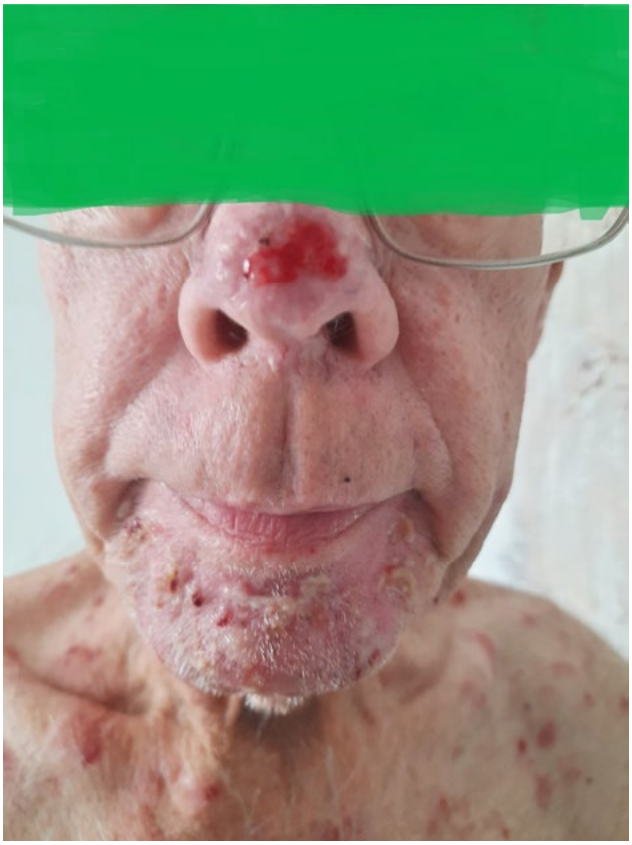

Figure 2: Clinical Features of Bullous Pemphigoid, Large Eroded Bullae on the Tip of the Nose with Multiple Smaller Bulla Over the Chin

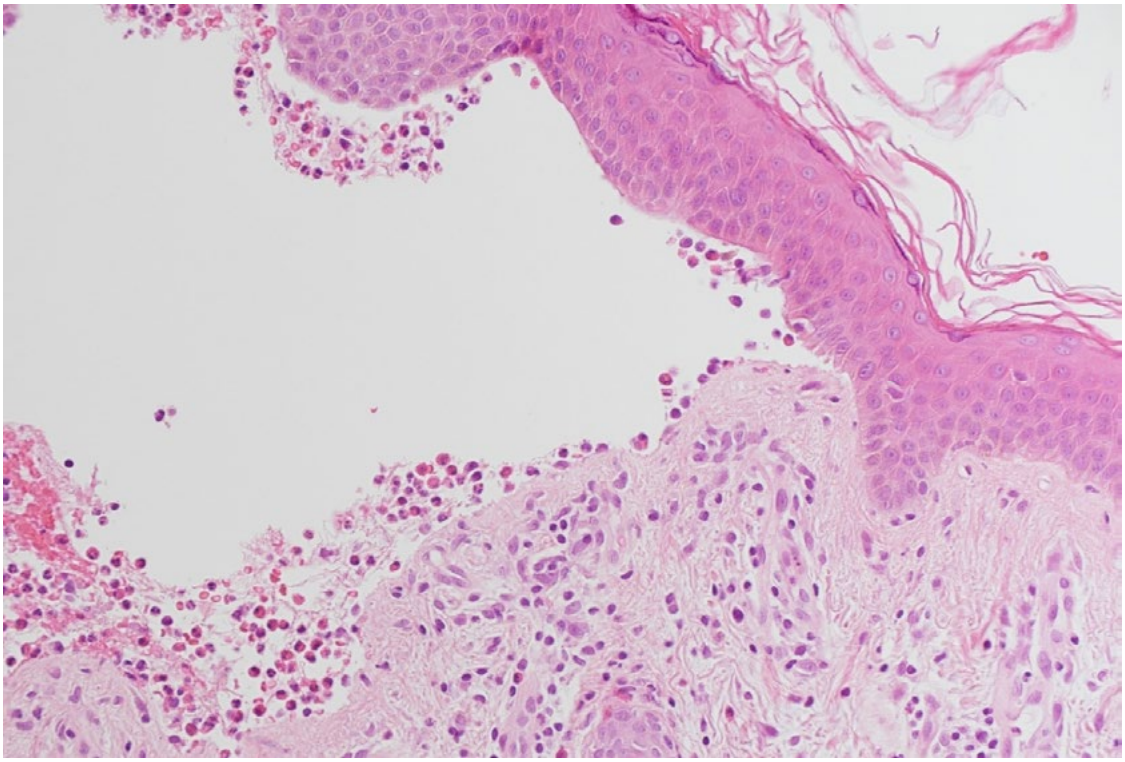

Figure 3: Microphotograph of The Skin Rash Biopsy Showing a Subepidermal Vesicle, Containing Eosinophil-Rich Inflammatory Cellularity. H & E; 200X

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